REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application, in light of the following remarks and pursuant to 37 C.F.R. § 1.112, are respectfully requested.

By the present amendment, claims 7-8, 12, 15-16, 21-22 and 26-32 have been cancelled, without prejudice or disclaimer to the subject matter disclosed therein. Furthermore, claims 6, 9, 11, 13, 14, 17, 19, 20, and 23-25 have been amended. Specifically, claim 6 has been amended to recite that the composition is a liquid. Support for this amendment to claim 6 can be found, for example, throughout the examples of the specification as filed, specifically in Example 1 on pages 13 and 14, wherein the OCIF and polysaccharide are dissolved in a solution when an injection formulation is prepared. The claims have also been amended to recite specific polysaccharides that can be used. Support for this amendment to the claim can be found, for example, on page 6, lines 15-24, of the specification as filed. Claims 6, 9-11, 13-14, 17-20, and 23-25 have been amended to remove the phrase "or a homolog thereof." New claims 33-35 recite compositions comprising OCIF homologs, and methods of using the compositions. New claims 33-35 find support in claims 1-5 as originally filed, and throughout the specification as filed. New claims 36 and 37 recite a lyophilized OCIF composition and methods of preparing a lyophilized composition, respectively. New claims 52 and 53 recite a lyophilized OCIF homolog composition and methods of preparing a lyophilized OCIF homolog composition. Support for new claims 36 and 37 and 52 and 53 may be found, for example, on page 8, lines 10-13, of the specification as filed. New claims 38 and 39 are directed to the methods of claims 13 and 20, respectively, in which the OCIF is lyophilized. Support for new claims 38 and 39 can be found, for example, throughout the Examples in the specification as filed. New claims 40 and 54 are directed to methods for lowering serum calcium levels. New claims 40 and 54 find support, for example, in Example 8 (on pages 22 and 23 of the specification as filed), and throughout the specification as filed. New claims 46 and 55 are directed to methods for prolonging the persistence of human OCIF protein in a subject. New claims 46 and 55 find support, for example, in Example 7 (on pages 21 and 22 of the specification as filed), and throughout the

specification as filed. Finally, the claims have been amended to correct obvious typographical errors. No new matter enters by way of these amendments.

Claim Objections

Claims 8, 12, 16, 22, 24, 28 and 32 were objected to for containing typographical errors. By the present amendment, each of these claims has been amended to correct these obvious errors. In light of the amendment, the objections to the claims are rendered moot.

Obviousness Type Double Patenting

Claims 6-32 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as purportedly being unpatentable over claims 1-3, 7-13, 27, 30-33, 37-43, 57-60 and 64-70 of co-pending U.S. Appl. Ser. No. 10/183,091 and claims 1-3, 7-13, 27, 30-33, 37-43, 57-60, and 64-70 of U.S. Appl. Ser. No. 10/364,045.

Applicants request that the Examiner holds these rejections in abeyance until allowable subject matter is indicated in the present application.

Rejection of Claims 6-32 Under 35 U.S.C. § 112, First Paragraph

Claims 6-32 have been rejected under 35 U.S.C. § 112, first paragraph, for purportedly not being enabled for a medicinal composition comprising a homolog of human OCIF or non-precipitated human OCIF and a polysaccharide, methods of enhancing the activity of an OCIF homolog, and a method for treating all diseases of bone-pathobolism comprising administering a composition comprising a human OCIF or an OCIF homolog and a polysaccharide. Applicants disagree with the Examiner and for at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

Initially, Applicants would like to thank the Examiner for his acknowledgement that the specification does enable a medicinal composition comprising human osteoclastogenesis inhibitory factor (OCIF) or non-precipitated human OCIF, or a defined homolog such as OCIF2,

OCIF3, OCIF4 or OCIF5 and a defined polysaccharide such as heparin, dextran sulfate, pectin or carrageenan; and a method of enhancing the activity of the OCIF, or a defined homolog of OCIF, by administering the OCIF or the homolog together with the polysaccharide; and a method for treating a specific bone-pathobolism such as hypercalcemia comprising administering said enabled composition; and a sustained-released composition comprising OCIF and a defined polysaccharide.

Claims 6, 9-11, 13-14, 17-20, 23-25 and 33-55 are directed to subject matter the Examiner has acknowledged is enabled. The amendments to these claims were made to expedite allowance of this application, and in no way acquiesces to the Examiner's assertion that the cancelled subject matter is non-enabled.

For example, claims 6 and 9-11, as amended, recite a liquid composition comprising OCIF and a polypeptide selected from the group consisting of: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, carrageenan, pectin, heparin, dextran, dextran sulfate, and sulfated glucan; claims 13-14 and 17-19, as amended, recite a method for enhancing the activity of OCIF comprising administering OCIF with a polysaccharide selected from the group consisting of: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, carrageenan, pectin, heparin, dextran, dextran sulfate, and sulfated glucan; new claim 33 recites a composition comprising an OCIF homolog selected from the group consisting of human OCIF2, OCIF3, OCIF4 and OCIF5 and a polysaccharide selected from the group consisting of: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, carrageenan, pectin, heparin, dextran, dextran sulfate, and sulfated glucan; new claim 34 recites a method for enhancing the activity of an OCIF homolog selected from the group consisting of human OCIF2, OCIF3, OCIF4 and OCIF5 comprising administering OCIF2, OCIF3, OCIF4 or OCIF5 with a polysaccharide selected from the group consisting of: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, carrageenan, pectin, heparin, dextran, dextran sulfate, and sulfated glucan; and new claim 35 recites a method of treating a bone pathobolism comprising administering a composition comprising an OCIF homolog selected from the group consisting of human OCIF2, OCIF3, OCIF4 and OCIF5 and a polysaccharide selected from the group consisting of: hyaluronic acid,

chondroitin sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, carrageenan, pectin, heparin, dextran, dextran sulfate, and sulfated glucan.

With regards to claims 20 and 23-25, applicants provide the following remarks. As amended, claims 20 and 23-25 recite a method of treating a bone pathobolism comprising administering a composition comprising OCIF and a polysaccharide selected from the group consisting of: hyaluronic acid, chondroitin sulfate, dermatan sulfate, heparan sulfate, keratan sulfate, carrageenan, pectin, heparin, dextran, dextran sulfate, and sulfated glucan. Osteoclasts play an important role in bone resorption, which causes an excessive flow of calcium into the blood. Therefore, an increase in calcium levels in the blood is indicative of an increase in bone resorption. Thus, if one were to decrease the rate of bone resorption (thereby increasing bone mineral density), the levels of calcium in the blood would also decrease. OCIF is known to inhibit differentiation of osteoclasts, and has been shown to be useful as a medicine for treating diseases in which bone resorption is elevated. See Simonet *et al.*, "Osteoprotegerin: A Novel Secreted Protein Involved in the Regulation of Bone Density," *Cell 89*:309-319 (1997), attached hereto as Exhibit A (also submitted with the Information Disclosure Statement and 1449, filed herewith). Simonet *et al.* disclose that OCIF (OPG) inhibits osteoclast differentiation (see the section starting on page 313, column 2, entitled "Recombinant OPG Blocks Osteoclastogenesis In Vitro") and suggests that OCIF (OPG) can be used for the treatment of osteoporosis, Paget's disease of the bone, hypercalcemia of malignancy, and osteolytic metastases, associated with increased osteoclast activity. To support this, Simonet *et al.* provide data which show OCIF protects Rats against ovariectomy-associated bone loss, and that OCIF increases bone density *in vivo*. See page 315, last paragraph in column 1, to page 316, first paragraph in column 1.

In light of these remarks, Applicants request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 7-9, 15-17, 20-25 and 27-29 Under 35 U.S.C. § 112, Second Paragraph

Claims 7-9, 15-17, 20-25 and 27-29 have been rejected under 35 U.S.C. § 112, second paragraph, for purportedly being indefinite. For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

Claims 7-9, 15-17, 21-23 and 27-29 have been rejected for purportedly using an improper Markush group. In order to expedite prosecution of this application, Applicants have removed the phrase "and combinations thereof" from the claims. A composition "comprising" human OCIF and a listed polysaccharide is open to include other ingredients, such as additional polysaccharides, including those listed in the Markush group.

Claims 20-25 have been rejected for purportedly lacking essential steps, specifically how much of the OCIF protein and polysaccharide are administered and the resulting effect of administration. While Applicants disagree, to facilitate prosecution claims 20 and 23-25 have been amended (claims 21 and 22 have been cancelled) to recite administering to a subject a composition comprising an amount of human osteoclastogenesis inhibitory factor (OCIF) protein and a polysaccharide, effective in combination for increasing bone density.

In light of these remarks, Applicants respectfully request withdrawal of these rejections under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 6-9 and 12 Under 35 U.S.C. § 102(a)

Claims 6-9 and 12 have been rejected under 35 U.S.C. § 102(a) for purportedly being anticipated by Goldenberg *et al.* (WO 98/46211). For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

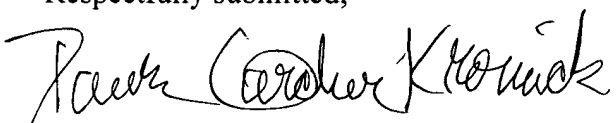
As noted by the Examiner, Goldenberg *et al.* disclose a gel composition comprising an aliginate gel matrix comprising a precipitated biologically active agent and a polysaccharide. The composition of Goldenberg *et al.* is not a liquid solution. Claims 6 and 8-9, as amended, (claims 7 and 12 have been cancelled) recite that the composition comprising human OCIF protein and a polysaccharide is a liquid composition. Therefore, the composition of the claimed invention and that disclosed by Goldenberg *et al.* are clearly different, and thus the claimed composition is not anticipated by the disclosure of Goldenberg *et al.*

In light of these remarks, withdrawal of this rejection under 35 U.S.C. § 102(a) is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants believe that the application is in condition for allowance and solicit a Notice of Allowance indicating such at the earliest possible time. The Examiner is encouraged to contact the undersigned should any additional information be necessary.

Respectfully submitted,



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